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Applicant:	Gill	Examiner:	J. Tung
Serial No.:	09/834822	Group Art Unit:	1637
Filed:	April 13, 2001	Docket No.:	7500.360US01
Title:	IMPROVEMENTS IN AND RELATING TO ANALYSIS OF DNA SAMPLES		

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office, Fax No. 703.872.9306 on December 30, 2003.

By: 

Name: Michael Hansen

**RESPONSE TO RESTRICTION REQUIREMENT**

Mail Stop Non-Fee Amendments  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In response to the Office Action mailed October 1, 2003, please amend the above-identified application as follows:

**Amendments to the Claims** are reflected in the listing of claims that begins on page 2 of this paper.

**Remarks** begin on page 10 of this paper.

**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1. (Currently Amended) A method of comparing one or more reference samples of DNA ~~in which the reference samples are~~ from known individuals and/or associated with other known factors with at least part of a test sample of DNA from a known individual and/or be associated with one or more other known factors, the method including:-  
the determination of the identity of the alleles present at a locus for the DNA in the test sample, the determination defining an individual test result, the determination being performed for a plurality of loci to give a plurality of individual test results, the consideration of one of the plurality of individual test results against the individual reference result of one of the reference samples for the respective loci, the consideration involving an expression of the probability that the individual reference result for that locus could lead by various possible routes to the individual test result for that locus, the possible routes to the individual test result including routes where spurious information contributes to the individual test result, the expression of the probability is a probability function and the probability function includes a probability that contamination may occur, a probability that stutter may occur, a probability that allele dropout may occur, and a probability that artifact reporting may occur; the consideration being repeated for a plurality of loci, the expressions of probability that the individual reference result could lead to the individual test result for the plurality of loci being combined to give an expression of the probability that the test sample matches the reference sample by calculating a likelihood ratio.

2. (Original) A method of comparing one or more reference samples of DNA with at least part of a test sample of DNA, the method including: the determination of the identity of the alleles present at a locus for the DNA in the test sample, the determination defining an individual test result, the determination being performed for a plurality of loci to give a plurality of individual test results, the consideration of one of the plurality of individual test results against the individual reference result of one of the reference samples for the respective

loci, the consideration involving an expression of the probability that the individual reference result for that locus could lead by various possible routes to the individual test result for that locus, the possible routes to the individual test result including routes where spurious information contributes to the individual test result; the consideration being repeated for a plurality of loci, the expressions of probability that the individual reference result could lead to the individual test result for the plurality of loci being combined to give an expression of the probability that the test sample matches the reference sample by calculating a likelihood ratio.

3. (Original) A method according to claim 1 in which the reference samples are from known individuals and/or associated with other known factors, such as locations, items or events.

4. (Original) A method according to claim 1 in which the test sample is from a known individual and/or be associated with one or more other known factors, such as a location, item or event the sample was recovered from.

5. (Original) A method according to claim 1 in which the consideration involves the determination of a likelihood ratio, the likelihood ratio accounting for the probability of the individual sample result arising from the individual reference result against the probability of the individual sample result arising from other than the individual reference result.

6. (Original) A method according to claim 1 in which the consideration involves the probability of the individual test result arising given that individual reference result, including through spurious information occurrence, for each individual test result, divided by the product of the probability of the individual test result arising from other than the individual reference result, including through spurious information occurrence, and the frequency of that individual reference result in a population, for each individual test result.

7. (Original) A method according to claim 1 in which in order to evaluated a mixture for a known and unknown contributor scenario, the likelihood ratio is the probability of the individual test result arising from an individual stored result, and other than the individual

stored result divided by the probability of the individual test result arising from other than the individual stored result and from other than the individual stored result.

8. (Original) A method according to claim 1 in which the probability of observation of alleles is calculated from the frequency of occurrence in relevant populations and used in the consideration.

9. (Original) A method according to claim 1 in which, where contamination is necessary to lead to the individual test result the probability includes a probability term for spurious allele occurrence.

10. (Original) A method according to claim 1 in which, where contamination must not occur to lead to the individual test result the probability includes a probability term for spurious allele non-occurrence.

11. (Original) A method according to claim 1 in which, where stutter is necessary to lead to the individual test result the probability includes a probability term for stutter occurrence.

12. (Original) A method according to claim 1 in which, where stutter must not occur to lead to the individual test result the probability includes a probability term for stutter non-occurrence.

13. (Original) A method according to claim 1 in which, where allele dropout is necessary to lead to the individual test result the probability includes a probability term for allele dropout occurrence.

14. (Original) A method according to claim 1 in which, where allele dropout must not occur to lead to the individual test result the probability includes a probability term for allele dropout non-occurrence.

15. (Original) A method according to claim 1 in which, where artifact reporting is necessary to lead to the individual test result the probability includes a probability term for artifact reporting occurrence.

16. (Original) A method according to claim 1 in which, where artifact reporting must not occur to lead to the individual test result the probability includes a probability term for artifact reporting non-occurrence.

17. (Original) A method according to claim 1 in which the probability function includes a probability that contamination may occur, the probability that contamination may occur being determined by one or more control determinations.

18. (Original) A method according to claim 1 in which the probability function includes a probability that stutter may occur, the probability that stutter may occur being determined by one or more control determinations.

19. (Original) A method according to claim 1 in which the probability function includes a probability that allele dropout may occur, the probability that allele dropout may occur being determined by one or more control determinations.

20. (Original) A method according to claim 1 in which, the probability function includes a probability that artifact reporting may occur, the probability that artifact reporting may occur being determined by one or more control determinations.

21. (Original) A method according to claim 1 in which the consideration is applied to all loci for which individual stored results and individual test results exist.

22. (Original) A method according to claim 1 in which the combination of probabilities produced by the respective considerations is obtained by multiplying the probabilities together.

23. (Original) A method according to claim 1 in which two or more different determinations of the identities of the alleles in the test sample are performed, the method of claim 2 being applied to each set of individual test results thereby obtained, the expression of a likelihood ratio for respective sets of individual test results being considered against one another and/or combined.

24. (Currently Amended) A method of indicating a likelihood ratio that evaluates that at least a part of a DNA test sample arose from a known source, the method involving:

the determination of the identity of the alleles present at the locus for the DNA from the known source;

the determination of at least some of the theoretical allele identities which could have produced a given individual test result, these identities forming the individual reference results;

one of the theoretical allele identities being the identity determined for that locus for the known source;

one or more determinations of the identity of the alleles present at a locus for the DNA in the test sample, each determination defining an individual test result;

~~the determination of at least some of the theoretical allele identities which could have produced a given individual test result, these identities forming the individual reference results;~~

~~the determination of the identity of the alleles present at the locus for the DNA from the known source;~~

~~one of the theoretical allele identities being the identity determined for that locus for the known source;~~

the provision of a probability function for each individual reference result considered which is representative of at least some of the various possible routes by which that given individual reference result may lead to the given individual test result, that probability function further being representative of the likelihood of that individual reference result's occurrence and the possible routes to the individual test result which includes routes where spurious information contributes, this probability function defining the theoretical probability functions;

the theoretical probability functions for different individual reference results being combined to give an indication of the various ways in which the given individual test result could be reached, this combination forming the combined theoretical probability function; the

provision of a probability function for the individual reference result matching the known source's identity, which is representative of the manner in which that individual reference result leads to the individual test result, this forming the known sources theoretical function;

the known source's theoretical function and combined theoretical function being considered together to calculate the likelihood ratio.

25. (Original) A method according to claim 24 in which at least part of a DNA sample refers to one source of a multi-source or mixed sample.

26. (Original) A method according to claim 24 in which the known source refers to a known individual and/or be associated with one or more other known factors, such as a location, item or event the sample was recovered from.

27. (Original) A method according to claim 24 in which the theoretical identities are determined from the alleles indicated in the individual test result, those theoretical identities which could reasonably lead to the individual test result being determined.

28. (Original) A method according to claim 24 in which the provision of a probability function involves the probability of getting that individual test result in any way, including through spurious information occurrence, and the frequency of that theoretical identity in a population, for each individual test result.

29. (Original) A method according to claim 24 in which the theoretical probability function for each individual reference result theoretical identity is defined in part by a probability for that individual reference results identity occurrence in a population.

30. (Original) A method according to claim 24 in which the theoretical probability function for each individual reference result is defined in part by a probability for the various occurrences which would result in that individual reference result giving the individual test result.

31. (Original) A method according to claims 24 in which theoretical probability functions are provided to account for each of the individual test results determined for a locus in the aforementioned manner.

32. (Original) A method according to claim 30 in which the theoretical probability functions for each individual test result given an individual reference result are combined.

33. (Original) A method according to claim 24 where contamination is necessary to lead to the individual test result the probability includes a probability term for spurious allele occurrence and/or where contamination must not occur to lead to the individual test result the probability includes a probability term for spurious allele non-occurrence and/or where stutter is necessary to lead to the individual test result the probability includes a probability term for stutter occurrence and/or where stutter must not occur to lead to the individual test result the probability includes a probability term for stutter non-occurrence and/or where allele dropout is necessary to lead to the individual test result the probability includes a probability term for allele dropout occurrence and/or where allele dropout must not occur to lead to the individual test result the probability includes a probability term for allele dropout non-occurrence and/or where artifact reporting is necessary to lead to the individual test result the probability includes a probability term for artifact reporting occurrence and/or where artifact reporting must not occur to lead to the individual test result the probability includes a probability term for artifact reporting non-occurrence.

34. (Original) A method according to claim 24 in which the various possible routes for the individual reference result giving the individual test result include contamination giving one or more alleles in the individual test result not present in the individual reference result.

35. (Original) A method according to claim 24 in which the various possible routes for the individual reference result giving the individual test result include stutter giving

one or more alleles in the individual test result not present in the individual reference result.

36. (Original) A method according to claim 24 in which the various possible routes for the individual reference result giving the individual test result include amplification of artifacts giving one or more alleles in the individual test result not present in the individual reference result.

37. (Original) A method according to claim 24 in which the various possible routes for the individual reference result giving the individual test result include allele drop out giving one or more alleles missing in the individual test result present in the individual reference result.

38. (Original) A method according to claim 24 in which the theoretical probability functions are combined to give the overall combined theoretical probability function by summing the theoretical probability functions together.

39. (Original) A method according to claim 24 in which the provision of the probability function for the individual reference involves the probability of getting that individual test result given that individual reference result, including through spurious information occurrence, for each individual test result.

40. (Original) A method according to claim 24 in which the likelihood ratio accounts for the probability that a given individual reference result/theoretical identity leads to the individual test result against the probability that the individual test result was lead to in another way.

### REMARKS

In response to the restriction requirement mailed October 1, 2003, Applicant offers the following remarks and amendments. Claims 1 and 24 were amended herein. Applicant respectfully submits that the amendments do not introduce any new matter. Favorable reconsideration is respectfully requested in light of the amendments and remarks submitted herein.

The Examiner has requested restriction of examination between two groups of claims. Group I comprises claims 1 through 23 apparently drawn to a method of comparing one or more reference samples of DNA in which the method includes the determination of the identity of alleles at a locus in the test sample, apparently classified in class 435, subclass 6. Group II comprises claims 24 through 40 apparently drawn to a method of indicating a likelihood ratio involving determining of at least some of the theoretical allele identities, apparently classified in class 435, subclass 6.

Applicant respectfully submits that the restriction requirement is improper and should be withdrawn because claim 24 is nothing more than a more explicit statement of the more general claim 1, and claim 2. This commonality can be seen from the explanation of the claims contained at least from page 30, paragraph 2 and ending at page 31, paragraph 3.

With respect to claim 24, identities for the alleles present in the test sample are determined using an analysis apparatus - set A of Figure 2. This set of results is not subject to any form of screening, and becomes set B for the subsequent comparison/likelihood ratio determination.

The identity of the alleles present at the same locus for the DNA from the known source against which the test sample is being considered is also determined experimentally. One of the theoretical alleles is then set to be the same identity determined for that locus from the known source. This is only one of a number of individual reference results against which a comparison is made, however. Hence, the methodology also involves the determination of other theoretical allele identities, which could have produced the individual test result, the individual reference results. All of these are set C results, in effect, against which a comparison is made.

In a comparison process, the individual test result, set B, is considered against an individual reference result, set C, in a number of repeats of the process. In one of the set Cs, the allele identities correspond to the actual known source allele identities.

In each case, the methodology accounts for the probability that the identities present in set C could have given rise to the identities present in set B by virtue of contamination, stutter allele dropout, etc. As well as accounting for the route, the consideration also involves a measure of the likelihood of that route occurring. The likelihood of the individual reference result corresponding to the identities for the actual known source, "the known sources theoretical function", is considered in relation to "the combined theoretical probability function" (which represents all of the possible ways in which all of the individual reference results could have given rise to the individual test results). The known sources theoretical function then becomes the numerator in the likelihood ratio with the combined theoretical function being the denominator (as per the equation on page 31).

The same considerations are involved in the methods of claims 1 and 2, but the steps are more generically defined therein. Thus, rather than establishing the likelihood ratio, the claims merely refer to making a comparison. Further in claim 1, the "one or more reference samples from known individuals" is analogous to the known source of claim 24. The method of claim 1 includes determining the alleles for the test sample and therefore individual test results are obtained. The individual test results are considered against an individual reference result, which reflects the reference sample identities. Just as with claim 24, the consideration reflects the different routes by which the individual reference result in question could have given rise to the individual test result. The expression of the probability of this occurrence, extended across multiple loci for which the reference sample and test sample are considered, allows an overall probability that the individual reference result could lead to the individual test result being established.

As a result, Applicant believes, given the clarifications made to claims 1 and 24 that they do relate to the same invention. In essence, claim 24 could be seen as claim 1 combined with claims 3 and 5.

**However, if the Examiner does not find the above convincing, Applicant respectfully elects Group I, comprising claims 1 through 23, with traverse. Favorable consideration of all claims is respectfully solicited.**

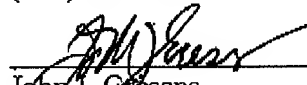
### Conclusion

If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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Date: December 30, 2003

  
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